Remarks

Independent claims 1 and 16 are amended to improve clarity and address the issues raised in the Office Action. Similarly, dependent claims 2, 3, 17, and 18 are amended to correspond better to the independent claims and improve clarity. No new matter is added by these amendments.

All pending claims are rejected as indefinite and unclear under **35 U.S.C. § 112, second paragraph.** No other rejections remain. The rejection is respectfully traversed.

The Office Action states that the claims are "confusing overall because a clear nexus between the steps is unclear. Specifically, it is unclear how the claim method operates to detect and determine species of eubacterial DNA in a sample." The preamble has been amended to correspond more closely to the last two steps of the method. It is respectfully submitted that the last two steps of the claims ("detecting presence of eubacteria…" and "determining presence of the first species…") provide nexus between all of the claim elements and steps, as well as the preamble.

Particular sub-issues raised are noted below.

1. **Relevance of *S. aureus* 16S rRNA gene.** This gene is used as a reference to define the primers. The primers are complementary to this gene. The primers, when used in a PCR reaction, will amplify this gene, if it is present. However, the primers will also amplify the 16S rRNA genes from other eubacteria if they are present in the sample to provide template. The PCR primers "prime virtually universally across species of eubacterial 16S rRNA genes." See [20]. Thus, if *S. aureus* is not present in the sample, the method will still be operative. The presence of *S. aureus* in the sample is <u>not</u> a requirement for determining various eubacterial species.
2. **Segments of the *S. aureus* amplified by the primers.** The definition of the

primers is based on what segment of *S. aureus* 16S rRNA they amplify. This definition has been amended to specify that the primers are "complementary to two hybridizing regions of a *S. aureus* 16S rRNA gene." The hybridizing regions are defined as flanking a segment comprising a conserved and a divergent region.[1] Because the primer-hybridizing regions flank the segment comprising a conserved and a divergent region, they will amplify the conserved and divergent regions in a PCR reaction, as is known in the art.[2] "The amplicon that the primers amplify contains both a conserved region and a divergent region." Specification at [20]. Thus the characteristics of the primers are that they are complementary to *S. aureus* 16S rRNA gene and they flank a segment within that gene which comprises a conserved and a divergent region. Thus the primers will not amplify ***any*** segment of a 16S rRNA, but will amplify a segment comprising a conserved and a divergent region. Examples of segments which could be amplified by the primers are provided in the application as filed and in the dependent claims. One such segment comprises nucleotides 890 to 1051 of *S. aureus* 16S rRNA gene. See specification at [26] and claim 4. One conserved region comprises nucleotides 1002 to 1024 of *S. aureus* 16S rRNA gene. See claim 5. One divergent region comprises nucleotides 945 to 978 of *S. aureus* 16S rRNA gene. See claim 5. An example of a pair of primers is provided in SEQ ID NO: 1 and 2. These examples are illustrative. Others can be used as well that have the recited properties.

3. **Nexus between presence or absence of *S. aureus* and the hybridization of probes to *B. japonicum*.** Neither *S. aureus* nor *B. japonicum* must be present in a

[1] The conserved region is defined as comprising at least 18 contiguous nucleotides which are at least 80 % identical among at least 10 eubacterial species. The divergent region is defined as comprising at least 10 contiguous nucleotides and differs by at least 3 nucleotides from a second divergent region found in a *B. japonicum* 16S rRNA gene.

[2] The hybridizing regions to which the primers are complementary form the ends of the amplified segment. The hybridizing regions may be external to or overlap with one or both of the conserved or divergent regions.

sample for the method to operate. The 16S rRNA genes of these species are merely used as reference sequences to define "conserved" and "divergent" regions within eubacterial 16S rRNA genes. The sample will typically have an unknown eubacterium in it, and the method will operate to detect and identify that eubacterium. The first probe should detect any eubacterium; the first probe hybridizes to the conserved region. The species of the eubacterium will be identified (*i.e.*, "determining presence of the first species") if the second probe hybridizes to a divergent region within the eubacterium's 16S rRNA. The claims do not require hybridization of the first or second probe to *S. aureus* or to *B. japonicum*. These species are merely used to provide reference sequences in comparison to which the conserved and divergent regions of rRNA genes are defined.

It is respectfully submitted that the claims are clear and definite as amended. Applicants request an in-person interview with the examiner if any questions remain with respect to the claim language.

Respectfully submitted,

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